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Generation and validation of MIR-142 knock out mice

Shrestha A., Carraro G., El Agha E., Mukhametshina R., Chao C., Rizvanov A., Barreto G., Bellusci S., Kalinichenko V.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2015 Shrestha et al.This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. microRNA-142 (miR-142) is an important regulator of many biological processes and associated signaling pathways during embryonic development, homeostasis and disease. The miR-142 hairpin gives rise to the "guide strand" miR-142-3p and the sister "passenger" strand miR-142-5p. miR-142-3p has been shown to play critical, non-redundant functions in the development of the hematopoietic lineage. We have recently reported that miR-142-3p is critical for the control of Wnt signaling in the mesenchyme of the developing lung. miR-142-5p has been proposed to control adaptive growth in cardiomyocytes postnatally and its increase is associated with extensive apoptosis and cardiac dysfunction in a murine heart failure model. Using homologous recombination, we now report the generation and validation of miR-142-null mice. miR-142-null mice show a significant decrease in th expression levels of both the 3p and 5p isoforms. The expression of Bzrap1, a gene immediately flanking miR-142 is not altered while the expression of a long non-coding RNA embedded within the miR-142 gene is decreased. miR-142-null newborn pups appear normal and are normally represented indicating absence of embryonic lethality. At embryonic day 18.5, miR-142-null lungs display increased Wnt signaling associated with the up-regulation of Apc and p300, two previously reported targets of miR-142-3p and -5p, respectively. Adult miR-142-null animals display impaired hematopoietic lineage formation identical to previously reported miR-142 gene trap knockdown mice. We report, for the first time, the homologous recombination-based miR-142-null mice that will be useful for the scientific community working on the diverse biological functions of miR-142.

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